

### Remarks

Claims 1-5, 21, 25-27, and 30-39 have been cancelled without disclaimer of or prejudice to the underlying subject matter. This application presently contains claims 28 and 29.

Applicants thank the Examiner for granting the interview of September 4, and for indicating during the interview that claims 28 and 29 may be allowable, pending consideration of Applicants' written Response to the Office Action mailed May 21, 2003.

#### *A. Objection to Priority Claim*

Applicants respectfully note that the Office Action mailed October 3, 2002 contained an Objection to Priority Claim. Applicants responded to the Objection to Priority Claim as part of the Response to the Office Action mailed October 3, 2002. Applicants respectfully note that the Office Action mailed May 21, 2003 does not address Applicants' response to the Office's Objection to Priority Claim. Applicants therefore reiterate herein their prior response to the Office's Objection to Priority Claim.

In the Office Action dated October 3, 2002, the Office alleged that Applicants have failed to comply with the formalities for claiming priority, by failing to provide a specific reference to the claimed prior application in the first sentence of the specification. Office Action at page 2. Applicants respectfully point out that, a priority claim to provisional application 60/142,981, filed 07/12/1999, was properly made in the transmittal letter submitted with this application on July 11, 2000. In addition, a Preliminary Amendment was filed September 17, 2001, to amend the specification to reflect said priority claim. Copies of the July 11, 2000 transmittal letter, and the September 17, 2001 Preliminary Amendment, each with the accompanying stamped postcard, are enclosed for the Examiner's reference. Courtesy copies of the Information Disclosure Statement, Form PTO-1449 and accompanying stamped postcard, also filed on September 17, 2001, are also included and brought to the Examiner's attention. As this Information Disclosure Statement was timely filed on September 17, 2001, Applicants do not believe any additional fees are due in conjunction with this submission. Applicants respectfully

request that the Examiner indicates he has considered the references cited by initializing the references in the 1449 and returning the Examiner-initialed 1449 to Applicants' representatives.

***B. Rejections under 35 U.S.C. § 101***

Claims 21 and 33-39 stand rejected under 35 U.S.C. § 101 for an alleged lack of both "credible asserted utility" and "well-established utility." Final Action at page 2. The Office also alleges that "[t]he problem of assigning function from structure is further exacerbated by the fact that the prior art does not support a correlation between the structure of the nucleic acids of the claims and the claimed function of the invention." Final Action at page 2.

Applicants respectfully disagree that claims 21 and 33-39 are not supported by either a credible asserted utility or a well-established utility. However, in order to facilitate prosecution, Applicants have cancelled claims 21 and 33-39 without disclaimer of or prejudice to the underlying subject matter. Applicants therefore submit that the grounds for the rejection of claims 21 and 33-39 has been rendered moot. In light of these remarks, Applicants respectfully request withdrawal of these rejections.

***C. Written Description Rejections under 35 U.S.C. § 112, First Paragraph***

Claims 1, 3-5, 21, 25-28, and 30-39 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention at the time the application was filed. Final Action at page 3. The Office further alleges that "[t]he prior art does not support a correlation between the common structural feature of the invention and the claimed function of the claims." Final Action at page 3. Applicants respectfully disagree.

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d

1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). In accordance with this purpose, Applicants need not "describe," in the sense of Section 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed. Cir. 1989). A related and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985), quoting *In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

An adequate written description of a genus of nucleic acids may be achieved by means of a "recitation of a representative number of [nucleic acids], defined by nucleotide sequence...or of a recitation of structural features common to the members of the genus." *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). The structural feature relied upon to describe the claimed genus must be capable of distinguishing members of the claimed genus from non-members. *Id.*

Applicants respectfully submit that each genus encompassed by claims 1, 3-5, 21, 25-28, and 30-39 is supported by Applicants' disclosure of "structural features common to the members of the genus" – *i.e.*, the sequences of SEQ ID NOs: 1 and 622. The specification further provides descriptions of constructs comprising such nucleic acid molecules, and methods of preparing such constructs. *See, e.g.*, page 13, line 5 through page 16, line 24; page 28, line 5 through page 34, line 16; and page 49, line 9 through page 52, line 9.

Moreover, Applicants note that the sequence of SEQ ID NO: 622 provides sufficient written description support for claim 28, which is directed to an isolated nucleic acid molecule that encodes a protein comprising the amino acid sequence of SEQ ID NO: 622. Applicants submit that, because the genetic code is well-known, listing all of the isolated nucleic acid molecules that encode SEQ ID NO: 622 would simply require reverse translating the amino acid sequence to the nucleic acid sequence. Theoretically, one armed with only a pencil, paper and the genetic code could list all of the isolated nucleic acid molecules that encode SEQ ID NO:

622. Therefore, the sequence of SEQ ID NO: 622 should provide adequate written description support across the scope of all encoding nucleic acids.

Applicants further note that there is an important distinction between the issue of whether an amino acid sequence provides adequate **description** of **all** encoding nucleic acids, and the issue of whether an amino acid sequence renders obvious one single, specific DNA sequence while excluding the enormous number of other potential DNA sequences that could code for the same protein.<sup>1</sup> The *Deuel* court's statement that "the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein" is conceptually consistent with the principle that an amino acid sequence provides adequate written description support for all encoding nucleic acids. *In re Deuel*, 51 F.3d 1552, 1558, 34 USPQ2d 1210, 1215 (1995).

Applicants therefore respectfully disagree that the specification contains inadequate written description support for claims 1, 3-5, 21, 25-28, and 30-39. Nevertheless, in order to facilitate prosecution, Applicants have cancelled claims 1, 3-5, 21, 25-27, and 30-39 without disclaimer of or prejudice to the underlying subject matter.

With respect to claim 28, Applicants submit that for the foregoing reasons, one of ordinary skill in the art would recognize that at the time of filing Applicants were in possession of the claimed invention. Therefore Applicants respectfully request that the written description rejection of claim 28 under 35 U.S.C. §112, first paragraph, be withdrawn.

#### ***D. Enablement Rejections Under 35 U.S.C. § 112, First Paragraph***

Claims 1-5, 21, 25-27 and 28-39 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which is allegedly not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Final Action at page 3. The Office further alleges that "[i]n the absence of any well-defined phenotype or function associated

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<sup>1</sup> In the context of obviousness, "[a] prior art disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein." *In re Deuel*, 51 F.3d 1552, 1558, 34 USPQ2d 1210, 1215 (1995).

with an oxysterol-binding protein in yeast or plants the claims are not enabled.” Final Action at page 4. Applicants respectfully disagree.

Applicants respectfully submit that the specification discloses how to make and use the claimed invention. The specification describes many uses for SEQ ID NO: 1 – to identify the presence or absence of a polymorphism; to identify genetic elements such as promoters and transcriptional regulatory elements; as a hybridization probe for gene expression profiling, such as with microarray technology; and to enhance phytosterol levels in transgenic plants to provide nutritionally enhanced food products, including cholesterol-lowering products. *See, e.g.*, specification at pages 1-5; page 49, line 9 through page 58, line 7; and page 64, line 4 through page 67, line 2.

Applicants further submit that the specification also teaches one of skill in the art how to use the claimed inventions for these utilities. For example, Applicants note that it is standard practice to use nucleic acids of known sequence (*e.g.*, SEQ ID NO: 1) to perform gene expression analysis using methods such as microarray technology. Knowing that an RNA corresponding to the claimed nucleic acid molecule is expressed under certain conditions or in certain tissues or at certain levels is in itself useful. For example, such information is useful to detect and compare expression changes in tissue samples taken from organisms grown under different conditions, *e.g.*, drought stress, cold stress, exposure to pathogens, or exposure to chemical compounds. SEQ ID NO: 1 might be differentially expressed, for example, under one or more growth conditions that tend to induce expression changes in genes involved membrane fluidity, *e.g.*, growth at low temperatures, or in the presence of salt or chemicals. This is consistent with the observation that in yeast, mutants in the HES 1 gene have a cold-sensitive phenotype and are resistant to the chemical agent nystatin. *See, e.g.*, Jiang *et al.* at page 350, second full paragraph. Microarrays allow rapid, simultaneous expression analysis of thousands of sequences, and thus, informative *patterns* of expression are derived from the microarray expression data. For at least these reasons, Applicants respectfully submit that expression analysis is a use of SEQ ID NO: 1 in a real world context. Applicants further submit that the specification teaches one of skill in the art how to use SEQ ID NO: 1 for this purpose. *See, e.g.*, specification at page 64, line 4 through page 67, line 2 (describing use of SEQ ID NO: 1 for microarray analysis of gene expression profiles).

It is well-established law that “the enablement requirement is met if the description enables any mode of making and using the invention.” *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991).

Section 2164.02 of the MPEP states that “[c]ompliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed.” An invention need not be actually reduced to practice prior to filing. *Gould v. Quigg*, 822 F.2d 1074, 1078 3 U.S.P.Q.2d 1302, 1304 (Fed. Cir. 1987). An application disclosure provides sufficient enabling support if one of skill in the art can, using the state of the art and Applicant’s written disclosures, practice the invention in its full scope without undue experimentation. *See In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988); *John Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998).

The performance of routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404; *In re. Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976). Time and difficulty of experiments are not determinative if they are merely routine. M.P.E.P. § 2164.06, page 2100-186.

That *some* experimentation would be required to make and use the invention does not defeat enablement. Section 2164.06 of the MPEP states that “[t]ime and difficulty of experiments are not determinative if they are merely routine.” “The test is not merely quantitative, since a considerable amount of experimentation is possible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed.” M.P.E.P. § 2164.06 (emphasis added), *quoting In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

Moreover, Applicants respectfully submit that the application is also sufficiently enabled with respect to the production of nutritionally enhanced food products, including cholesterol-lowering products. The specification provides methods of preparing expression constructs, methods for transforming plants, as well as a method for screening transgenic plants for altered

phytosterols levels. *See, e.g.*, specification at pages 1-5; page 13, line 5 through page 16, line 24; page 28, line 5 through page 42, line 26; page 49, line 9 through page 52, line 9; and Example 3. Applicants submit that the specification provides sufficient disclosure to enable the invention, because techniques for the production and screening of transgenic plants are well-known in the art, and the level of skill in the art is high.

Applicants also respectfully note that the Examiner has not provided **direct** evidence refuting the use of the **specific** sequence of SEQ ID NO: 1 in the manner described in the specification. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement). As a result, Applicants respectfully submit that the Examiner has failed to meet the burden required to establish an enablement rejection.

Applicants have described at least four modes of making and using the invention. Any one of these modes alone is enough to satisfy the enablement requirement of Section 112. Because Applicants need only establish a single mode of making and using the invention to satisfy 35 U.S.C. § 112, and have done so in the present case, the premise of the rejection under Section 112 is incorrect.

Although Applicants respectfully disagree that claims 1-5, 21, 25-27 and 28-39 are not enabled, in order to facilitate prosecution, Applicants have cancelled claims 1-5, 21, 25-27 and 30-39 without disclaimer of or prejudice to the underlying subject matter. Applicants therefore submit that the grounds for the rejection on claims 1-5, 21, 25-27 and 30-39 has been rendered moot. In light of these remarks, Applicants respectfully request withdrawal of these rejections.

With respect to claims 28 and 29, Applicants submit that for the foregoing reasons, one of ordinary skill in the art would recognize that the specification as filed enables one skilled in the art to make and use the claimed invention. Therefore Applicants respectfully request that the enablement rejections under 35 U.S.C. §112, first paragraph, be withdrawn.

***E. Rejections under 35 U.S.C. § 112, Second Paragraph (Indefiniteness)******Rejection of Claims 1-5, 21, 34, 36, and 38***

Claims 1-5, 21, 34, 36, and 38 stand rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite in the recitation of the phrase "substantially purified." Final Action at pages 4-5. Applicants disagree.

Applicants have provided a definition for the phrase "specifically hybridizes." *See, e.g.*, specification at page 12, lines 14-20. Furthermore, Applicants point the Office to U.S. Patent 6,518,488, in which claim 1 recites "A substantially purified nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 1 or its complement."

Although Applicants disagree that claims 1-5, 21, 34, 36, and 38 are indefinite in the recitation of the phrase "substantially purified," in order to facilitate prosecution, Applicants have cancelled claims 1-5, 21, 34, 36, and 38 without disclaimer of or prejudice to the underlying subject matter. Applicants therefore submit that the grounds for the rejection of claims 1-5, 21, 34, 36, and 38 has been rendered moot. In light of these remarks, Applicants respectfully request withdrawal of this rejection.

***Rejection of Claims 3, 5, 30 and 32***

Claims 3, 5, 30 and 32 stand rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite in the recitation of the phrase "specifically hybridizes." Final Action at pages 5-6. Applicants disagree.

Applicants have provided a definition for the phrase "specifically hybridizes." *See, e.g.*, specification at page 17. Applicants respectfully disagree that claims 3, 5, 30 and 32 – when read in light of the definition in the specification – would not be understood by one of skill in the art.

Although Applicants disagree that claims 3, 5, 30 and 32 are indefinite in the recitation of the phrase "specifically hybridizes," in order to facilitate prosecution, Applicants have cancelled claims 3, 5, 30 and 32 without disclaimer of or prejudice to the underlying subject matter.



Applicants therefore submit that the grounds for the rejection of claims 3, 5, 30 and 32 has been rendered moot. In light of these remarks, Applicants respectfully request withdrawal of this rejection.

***F. Rejections under 35 U.S.C. § 102(b)***

Claims 1-5, 21, 34, 36, and 38 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Ji *et al.*, *Plant Physiology*, 104(2):453-459 (1994). The Office alleges that “[t]he claims do not recite any function for the claimed nucleic acid sequences and since the claims are indefinite as argued *supra* they are indeed anticipated by the prior art.” Final Action at page 6. Applicants respectfully traverse this rejection.

Applicants disagree with the Office’s implied assertion that the language of claims 1-5, 21, 34, 36, and 38 is so broad as to render these claims anticipated by *any disclosure* of an isolated soybean nucleic acid. Whatever else Ji *et al.* discloses, it does *not* disclose a substantially purified nucleic acid molecule comprising (a) the nucleic acid sequence of SEQ ID NO: 1; or (b) the amino acid sequence of SEQ ID NO: 622; or (c) a HES1 protein. Ji *et al.* at figure 3, page 456. Moreover, Applicants respectfully submit that this rejection has been overcome by the above arguments regarding the alleged indefiniteness of claims 1-5, 21, 34, 36, and 38 for the use of the phrase “substantially purified.”

Although Applicants disagree that claims 1-5, 21, 34, 36, and 38 are anticipated under 35 U.S.C. § 102(b) by Ji *et al.*, in order to facilitate prosecution, Applicants have cancelled claims 1-5, 21, 34, 36, and 38 without disclaimer of or prejudice to the underlying subject matter. Applicants therefore submit that the grounds for the rejection of claims 1-5, 21, 34, 36, and 38 has been rendered moot. In light of these remarks, Applicants respectfully request withdrawal of this rejection.

***G. Provisional Rejections for Obviousness-Type Double Patenting******Rejection of Claims 1-5, 21, and 25-26***

Claims 1-5, 21, and 25-26 stand provisionally rejected under 35 U.S.C. § 101 as allegedly claiming the same invention as that of claims 1-5, 21, 25 and 28 respectively of copending application number 10/030,537. Final Action at page 7. In order to facilitate prosecution, Applicants have cancelled claims 1-5, 21, 25 and 26 without disclaimer of or prejudice to the underlying subject matter. Applicants therefore respectfully submit that the grounds for the rejection of claims 1-5, 21, 25 and 26 has been rendered moot. In light of these remarks, Applicants respectfully request withdrawal of this rejection.

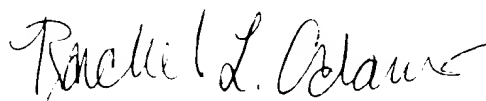
***Rejection of Claims 27 and 28-39***

Claims 27 and 28-39 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 26 of copending application number 10/030,537. The Office alleges that “the further purification of the “substantially purified” molecules of the copending application would have been obvious.” Final Action at pages 7-8. Upon indication of allowable subject matter, Applicants will file a preliminary amendment to cancel claim 26 of copending application number 10/030,537, without disclaimer of or prejudice to the underlying subject matter. Applicants therefore respectfully submit that the grounds for the rejection of claims 27 and 28-39 has been rendered moot. In light of these remarks, Applicants respectfully request withdrawal of this rejection.

**Conclusion**

In view of the above, each of the presently pending claims is believed to be in condition for immediate allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue. The Examiner is respectfully requested to contact Applicants' undersigned representative at 202.942.5512 to address any unresolved issues remaining in this application.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Rachel L. Adams", with a long horizontal flourish extending to the right.

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